8/8/05

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SUMMARY STATEMENT
(Privileged Communication)
Application Number: 1 R43 HD050805-01A1
Formerly: 1R43AI065089-01
RESNIC, DANIEL
STRATA VARIOUS PRODUCT DESIGN
311 NORTH ROBERTSON BLVD #318
BEVERLY HILLS, CA 90211

Review Group: ZRG1 AARR-G (15)
Center for Scientific Review Special Emphasis Panel
AIDS - EXP. REV.
Meeting Date: 07/13/2005
Council: OCT 2005 *PCC:* CRH -SK
Requested Start: 01/01/2006
Project Title: New Silicone Condom: Feasibility Study
SRG Action: Priority Score: 185
Human Subjects: 30-Human subjects involved - Certified, no SRG concerns
Animal Subjects: 30-Vertebrate animals involved - no SRG concerns noted
Gender:
Minority:
Children:
1A-Both genders, scientifically acceptable
1A-Minorities and non-minorities, scientifically acceptable
1A-Both Children and Adults, scientifically acceptable
Clinical Research - not NIH-defined Phase III Trial
Project Year; 1

TOTAL
Direct Costs Requested
$180,954

180,954
Estimated Total Cost
$180,954

$180,954

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

NEW INVESTIGATOR
ZRG1 AARR-G (15) 2 1 R43 HD050805-01A1
RESNIC, D
1R43HD050805-01A1 RESNIC, DANIEL

RESUME AND SUMMARY OF DISCUSSION: This revised Phase I SBIR application proposes to refine and test a condom made from silicone. They first will fabricate three prototypes to evaluate their structural properties and biocompatibility. Next they will test the condom's acceptability and performance with 10 heterosexual couples and finally they will compare it to standard latex condoms in 36 couples. This is an innovative application that may provide a needed alternative to latex condoms.

The applicant was very responsive to the prior reviews and the present application is much improved. One significant change was the plan now tests the condom as male device only, rather than a unisex device. The committee's high enthusiasm for this application was only slightly diminished by a lack of detailed information about the clinical trials.

DESCRIPTION (provided by applicant): The primary objective of this grant is to refine and test a prototype of the ORIGAMICondom™: a new condom made from silicone, a material that may offer better sensation and be less prone to breakage than latex or plastic. The ORIGAMI Condom will feature several technological innovations, including: 1) strong, heavy- gauge material that feels like human tissue, creating sensation instead of acting as a filter to it, 2) a loose fit for greater ORIGAMI, 3) a discrete scrotal retention band to reduce the likelihood of slippage, and 4) highly stretchable material for better fit and ORIGAMI. There are five specific aims: 1. Fabricate three prototypes of the ORIGAMI Condom™ from silicone using liquid injection molding. 2. Confirm that the Class VI medical grade silicone used in the ORIGAMI Condom™ remains biocompatible after the manufacturing process. The completed condoms will undergo laboratory testing for cytotoxicity, sensitization, irritation, and systemic toxicity. All three prototypes will be tested. 3. Assess the structural integrity of the ORIGAMI Condom™ by measuring tensile properties, leakage, permeability, airburst volume, and airburst pressure. All three prototypes will be tested. 4. Compare the safety, acceptability, and performance of the three ORIGAMI Condom™ prototypes. A "Feasibility and Design" study will be conducted with ten heterosexual couples. Each couple will use six condoms (two of each prototype), rate various subjective features of each condom, and report on any breakage, slippage, or adverse events they may experience. 5. Compare the safety, acceptability, and performance of the best ORIGAMI Condom™ prototype with a commercial male latex condom. A "Performance and Acceptability" study will be conducted with thirty-six couples. Each couple will use three ORIGAMI Condoms™ and three latex condoms, rate various subjective features of each condom, and report on any breakage, slippage, or adverse events they may experience. For sexually active couples, condoms used correctly and consistently are the most effective method available to reduce the risk of transmitting HIV and other sexually transmitted infections (STI). Unfortunately, many individuals find latex condoms unacceptable. The development of new and improved condoms is a key component in combating the HIV/AIDS crisis.

CRITIQUE 1:

Significance: This is a phase I application to refine and test a prototype of a silicone condom. It is highly significant in proposing to develop a condom that will potentially have a higher acceptance rate than the latex condom. Two primary benefits are advanced for silicone rather than latex: that it may provide better sensation and that it will be less prone to breakage. There would be a high level of significance to developing a condom with these characteristics if it led to increased condom use.

Approach: The steps proposed for testing this condom prototype are appropriate, beginning with pre-clinical test of biocompatibility and structural integrity, followed by assessment of feasibility and design, and evaluation of performance and acceptability. 0The applicant has been responsive to reviewer comments on the initial proposal. The most significant change is that the applicant now proposes to test the new condom as a male device only and not a unisex device. The original proposal sought to demonstrate the feasibility of two innovations: the silicone material and the unisex design. This step is quite responsive and represents an improvement in the application because serious concerns had been expressed with respect to the feasibility of the product for female use. This modification will further address the reviewer concern that the proposal was ambitious with respect of time and budget. However, concerns about completing the work within the allotted time and budget still exist, especially if it is necessary to revise the condom prototypes or address other problems. The applicant has added further biocompatibility tests at the request of the FDA. In addition, the investigator has added information concerning potential problems, including criteria that will be used to establish whether the new condom meets standards of acceptability in each of the two clinical trials.

A key claim of the applicant is that silicone will be less prone to breakage and stronger than latex condoms. If this is not the case, the new condom will not be as desirable as a latex condom, even if more acceptable with respect to sensation. Previous concerns were expressed that the new condom would be likely to break. These concerns would be more fully addressed if the investigator provided information on comparisons of latex to silicone in other relevant health applications and/or compared the silicone condom to a latex condom in the pre-clinical structural testing in order to establish comparability of the two products.

Previous reviewers cited lack of detail with respect to the clinical trials. The applicant has addressed this by providing more information. However, some concerns may be cited with respect to the methods to be followed. Although samples of the questionnaires to be administered are not provided, it appears that there needs to be more data to be collected from couples, as levels of mood, desire, and arousal may play significant roles in reactions to the condoms.

The procedure in the Performance and Acceptability Study (in which three condoms of each type are tested before crossing over to the other type) would seem to maximize the possibility that circumstances unrelated to type of condom would influence the sexual experience (e.g. couple is getting along well during one period of time, less so during another period of time), which might potentially affect condom acceptance.

It is not always clear whether information will be provided separately for each partner, for example on the Condom Use Report. It would seem preferable if this were the case. In addition, at the exit interview it appears that participants will be interviewed together. It might be preferable if interviews were conducted individually with partners, as one partner may tend to accede to the views of the other or may be inhibited with respect to expressing his or her own views with the partner present. This procedure will also permit greater confidentiality for each participant.

It is indicated in section 6.0 that statistical tests will be performed. However, there is no information provided on what these tests will be, or how it will be determined from the data collected whether breakage, slippage, failure rates and acceptability ratings differ among the three condom prototypes in the feasibility and design testing study and between silicone and latex condoms in the performance and acceptability study.

In section 7.0 various standards of acceptability for the condoms to be tested are provided. However, there is no justification provided for the decision to use these specific standards. For example, why is a rate of female genital discomfort less than 20% of the time is acceptable compared to a rate male genital discomfort less than 10% of the time?

Innovation: The proposal is highly innovative with respect to the material for condoms as well as design.

Investigators: The applicant is trained in product design and has significant experience in this area. He has brought together an extremely well qualified team.

Environment: The research environment and facilities to be used in the proposed tests appear appropriate, including Nelson Laboratories and the California Family Health Council. ZRG1 AARR-G (15) 4 1 R43 HD050805-01A1 RESNIC, D

Overall Evaluation: This is a potentially highly significant application. The applicant has been responsive to reviewer comments in modifying the design of the study such that the feasibility of the new condom will no longer be tested for unisex use. There is still some concern with respect to structural properties of the silicone condom. With further specification of procedures for clinical trials, questions arise concerning factors that may affect condom acceptability ratings, the potential need for separate data collection for individual partners, statistical testing of results, and justification for standards of acceptability.

Protection of Human Subjects from Research Risks: 4 Required Points: Additional risks to subjects include embarrassment in providing reactions to condoms and condom use. Male participants may experience embarrassment in recording or reporting penis size. Privacy and confidentiality risks include not only accidental disclosure of information by the researcher but also disclosure of information by the partner. The procedures listed under protection against risk only ensure confidentiality from researcher disclosure.

Gender, Minorities, and Children: Both women and men will be included. Minorities will be included. Children between the ages of 18 and 21 will be included. Data Safety & Monitoring Plan: A data safety and monitoring plan is included but could be addressed more fully.

CRITIQUE 2:

Significance: As stated by the author, condoms used correctly and consistently are the most effective method available to reduce the risk of transmitting STI's including HIV. However, many find latex condoms unappealing and unacceptable for multiple reasons including lack of sensation and latex allergies. This product would provide an alternative that would be stronger than latex condoms yet provide better sensation. The overall goal of this project is to refine and test a prototype of the ORIGAMI Condom, a new condom made from silicone. '

Approach: The PI has addressed the issues raised by previous reviewers including modification of the goals for Phase I, the currently proposed goals (test as male condom only, allow 8 months) are more reasonable. The PI also provided further detail about the product including information about the greater thickness of the ORIGAMI Condom compared to current latex condoms.

The current application states clear goals for both the first and second trail and has an alternative plan if the criteria are not met from the first trial.

The first trial (4 week study period) will recruit 10 couples to evaluate 2 condoms of each of the 3 prototypes for acceptability, safety, and performance. The criteria (breaks, slippage, genital disORIGAMI, etc) for the feasibility of the first trial are clear and allow for use of none of all three of the prototypes to proceed to the second trial.

The second trial will recruit 36 couples to compare the performance, acceptability, and safety of 3 condoms of the selected prototypes to 3 latex condoms.

Innovation: The author states that the ORIGAMI Condom will feature several technological innovations including 1) stronger, heavier material that feels like human tissue, creating sensation instead of filtering it, 2) a looser fit for greater ORIGAMI, 3) a discrete scrotal retention band to reduce slippage, and 4) a highly stretchable material for better fit and ORIGAMI. Additionally, the ORIGAMI Condom will be unlike current condoms on the market in three innovative ways a) reusable, therefore increasing use among those without ready access, b) used by males and females (will be further explored), and c) pop up rather than roll down, leading to shorter time to use and thus less interruption during the sex act.

Investigators: PI is the inventor and is well qualified to direct the design and evaluation of this product.

Environment: Acceptable

Overall Evaluation: This current application has addressed the issues raised by previous reviewers. The product addresses an important issue, has clear goals for Phase I, and has strong potential for commercialization.

Protection of Human Subjects from Research Risks: Acceptable
Inclusion of Women – 50%, Acceptable
Inclusion of Children – Excluded, Acceptable

CRITIQUE 3:

Significance: The objective of this study is to refine a prototype male silicone condom for clinical comparison with a commercially distributed male latex condom. Requisite pre-clinical testing is planned to determine physical strength parameters and chemical biocompatibility. If successfully marketed, this new condom may improve condom acceptability among non-condom users.

Approach: Considering that silicone is used in similar medical devices, it appears appropriate to consider this material for condoms. The rationale is based on the product's mechanical properties and the perceived acceptability and health benefits.

Innovation: This product, if proven acceptable for human use could revolutionize the male condom with respect to enjoyment while providing protection from disease and pregnancy. It is clear that alternative products are needed to promote condom use, and the Strata condom has the potential to enhance acceptance and use among those that engage in risky behaviors.

Investigators: The assembled team of investigators appears more than adequately qualified for this research. Mr. Resnic's imagination and desire to provide more acceptable and user-friendly products for consumers is admirable. Dr. Frezieres has a proven track record in condom clinical research and is most qualified to undertake this work.

Environment: The proposed collaboration between the listed organizations is appropriate for this research.

Response to Previous Review: The proposal discusses the plan for physical testing or characterization of the product. Although the test methods specified in the ASTM standards are appropriate for evaluating the prototypes, the methods may need modification to accommodate the 'ORIGAMI' design. There is not sufficient discussion of testing for the Scrotal Retention Strap. If the purpose of the strap is to prevent slippage, a strength/ breakage requirement must be prescribed. Also, a measurement or test to evaluate the function of the reservoir should be included. Section 3.0 – Pre-Clinical Testing must be expanded to fully describe the proposed testing. Deviations and/or modifications from standard test methods should be discussed.

Protection of Human Subjects from Research Risks: Acceptable
Inclusion of Women Plan: Acceptable
Inclusion of Minorities Plan: Acceptable
Inclusion of Children Plan: Acceptable

Overall Evaluation: This proposal is appropriate for selecting a suitable design for clinical study. However, the pre-clinical testing plan needs further refinement in that the proposal specifies 225 samples for physical testing; 20 for bacteriophage, and 108 for clinical use; total 373. However the budget suggests a total of 250 prototypes. Also, it is recommended that additional specimens be added for possible re-tests, particularly if modified tests are employed.

CRITIQUE 4:

Significance: The significance of the project is very high: more alternatives are needed to latex condoms, both because of allergy and acceptability issues. Silicone-based condoms may provide a reasonable alternative to latex condoms, providing additional comfort and sensitivity.

Approach: The investigator has clearly thought through many research and design issues. The study proposes to 1) fabricate 3 prototypes of a silicone-based condom; 2) perform pre-clinical testing, and 3) test products in phase 1 trials using heterosexual monogamous couples. The Background and Significance section is extremely brief and provides few references to back up many of the statements. In Section D, no information is provided on how various staff on this ambitious project will coordinate and exchange data with one another; this is especially concerning for the pre-clinical aspects of the study, which will be performed by a subcontractor.

Innovation: The proposal to develop a silicone-based condom is innovative.

Investigators: While having no experience in prior clinical studies, the investigator has assembled a well experienced research team. However, more information should be provided re: how the investigator plans to coordinate this team.

Environment: The environments described are adequate for the work being proposed.

Protection of Human Subjects from Research Risks: No specific information is provided with regard to a DSMB. More information is required on who will be assessing and recording adverse events.
Inclusion of Women Plan: Satisfactory
Inclusion of Minorities Plan: Satisfactory
Inclusion of Children Plan: Satisfactory

Overall Evaluation: An innovative, significant, ambitious proposal. Enthusiasm is somewhat dampened by timeline and lack of details regarding study coordination and procedures.
ZRG1 AARR-G (15) 7 1 R43 HD050805-01A1
RESNIC, D

THE FOLLOWING RESUME SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW ADMINISTRATOR TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE ON THE FOLLOWING ISSUES:
PROTECTION OF HUMAN SUBJECTS (Resume): ACCEPTABLE
INCLUSION OF WOMEN PLAN (Resume): ACCEPTABLE
INCLUSION OF MINORITIES PLAN (Resume): ACCEPTABLE
INCLUSION OF CHILDREN PLAN (Resume): ACCEPTABLE
VERTEBRATE ANIMAL (Resume): ACCEPTABLE
COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

MEETING ROSTER
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ZRG1 AARR-G (15) B
July 13, 2005

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